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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,625	06/02/2000	Carlos F. Barbas III	22908-1227B	6568

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EXAMINER

MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 11/04/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/586,625

Applicant(s)

BARBAS ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2002 .
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-35,37-46 and 69-73 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-35,37-46 and 69-73 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____ .
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12 .
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____ .

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DETAILED ACTION

Formal Matters

Claim 4 was cancelled, and claims 1, 5, 8, 13, 20, 22, 25, 32, 34, 39, 43 and 45 were amended in Paper No. 13, 8/20/2002. Claims 1-3, 5-35, 37-46, 69-73 are pending and under consideration.

Election/Restrictions

In Paper No. 10, 11/21/2001, Applicant elected without traverse Group I, claims 1-35, 37-46, 69-73. Applicant requests clarification of the Restriction Requirement of Paper No. 8, 9/11/2001. Groups I-XVIII are independent and distinct, each from the other, because they are products which possess characteristic differences in structure and function, and each has an independent utility, that is distinct for each invention which cannot be exchanged. Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. The generic claims have been examined, as well as SEQ ID NO: 1. Assuming, *arguendo*, that the generic claims are allowable, SEQ ID NOs: 2-18 will not be rejoined because they are independent and distinct inventions. This is in contrast to the elected species, where in all applications where a generic claim is found allowable, the application should be treated as indicated in MPEP § 809.02 (b), § 809.02 (c), or § 809.02 (e).

Response to Amendment and Arguments

Applicant's arguments filed 8/20/2002 have been fully considered but they are not persuasive for the reasons set forth below.

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The objection to claim 11 is withdrawn.

The rejection of claims 9, 13, 15, 16, 17, 18, 19 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substantially purified polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 1, does not reasonably provide enablement for a protein variant of SEQ ID NO: 1 has been withdrawn based on Applicant's arguments.

The rejection of claims 9, 13, 15, 16, 17, 18, 19 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention has been withdrawn based on Applicant's arguments.

The rejection of claims 39-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention has been withdrawn based on Applicant's arguments.

The rejection of claim 1, 8, 69 and dependent claims under 35 USC § 112 second paragraph for recitation of the term "modular portion" has been withdrawn based on Applicant's arguments.

The rejection of claims 1-3, 5-19, 23-24, 26-31, 69-73 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent no. 5,217,867 (Evans et al.) has been obviated by Applicant's amendment, and is thus withdrawn.

Claim Objections

Claim 25 is objected to because of the following informalities: They contain subject matter drawn to non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-35, 37-46, 69-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fusion protein comprising an amino acid sequence set forth in SEQ ID NO: 1, and fusion proteins comprising a zinc finger protein E2C(Sp1), B3B(Sp1) or B3C2(Sp1) and ERD, KRAB, KRAB, SID domains which bind the erbB-2 promoter, does not reasonably provide enablement for a protein variant of SEQ ID NO: 1, or a fusion protein comprising a ligand binding domain derived from an intracellular receptor wherein the nucleotide binding domain is derived from a zinc-finger peptide which binds a sequence of at least 3 nucleotides, or a variant of such a fusion protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-3, 5-35, 37-46, 69-73 are overly broad since insufficient guidance is provided as to which of the myriad of variant fusion polypeptides will retain the characteristics of functioning as a transcriptional regulator. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the

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protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the claims encompass variant and derivative fusion proteins and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

(1) the breadth of the claims - The claims are drawn to a fusion protein comprising a ligand binding domain derived from an intracellular receptor wherein the nucleotide binding domain is derived from a zinc-finger peptide which binds a sequence of at least 3 nucleotides, or a variant of such a fusion protein.

(2) the nature of the invention - The instant invention is a fusion protein comprising a ligand binding domain derived from an intracellular receptor wherein the nucleotide binding domain is derived from a zinc-finger peptide which binds a sequence of at least 3 nucleotides, or a variant of such a fusion protein.

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(3) the state of the prior art - The Voet reference demonstrates that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

(5) the level of predictability in the art - The Voet reference demonstrates the unpredictability of the protein art.

(6) the amount of direction provided by the inventor - Applicant has taught a fusion protein comprising an amino acid sequence set forth in SEQ ID NO: 1, and fusion proteins comprising a zinc finger protein E2C(Sp1), B3B(Sp1) or B3C2(Sp1) and ERD, KRAB, SID domains which bind the erbB-2 promoter.

(7) the existence of working examples - Working examples are only provided for a fusion protein comprising an amino acid sequence set forth in SEQ ID NO: 1, and fusion proteins comprising a zinc finger protein E2C(Sp1), B3B(Sp1) or B3C2(Sp1) and ERD, KRAB, KRAB, SID domains which bind the erbB-2 promoter.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The instant application teaches fusion proteins which bind the erbB2 promoter, but not to any other promoter. Thus, Thus the instant application is enabled for the genus of polydactyl zinc finger fusion proteins which bind the erbB2 promoter, but not to polydactyl zinc finger fusion proteins which bind to any other contiguous nucleotide sequences of at least 3 nucleotides, or a variant of such a fusion protein. Given the breadth of claims 1-3, 5-35, 37-46, 69-73 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification

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and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 1-3, 5-35, 37-46, 69-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to a protein variant of SEQ ID NO: 1, or a fusion protein comprising a ligand binding domain derived from an intracellular receptor wherein the nucleotide binding domain is derived from a zinc-finger peptide which binds a sequence of at least 3 nucleotides, or a variant of such a fusion protein. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

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A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In the instant case, Applicant has taught a fusion protein comprising an amino acid sequence set forth in SEQ ID NO: 1, and fusion proteins comprising a zinc finger protein E2C(Sp1), B3B(Sp1) or B3C2(Sp1) and ERD, KRAB, SID domains which bind the erbB-2 promoter. However, the instant application teaches fusion proteins which bind the erbB2 promoter, but not to any other promoter. Thus the instant application demonstrates possession of common elements of the genus of polydactyl zinc finger fusion proteins which bind the erbB2 promoter, but not to polydactyl zinc finger fusion proteins which bind to any other contiguous nucleotide sequences of at least 3 nucleotides, or a variant of such a fusion protein.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 37-46, 69-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record set forth in Paper No. 11, 2/8/2002.

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Claims 1, 8, 21, 22, 25, 32, 39, 43, 45 are indefinite in the recitation of the term "derived from".

It is unclear whether this term imposes a required limitation on the claim, such that it only encompasses, for example, polynucleotides amplified from human cDNA, or only sequences produced by digestion with restriction enzymes of DNA isolated from human tissue that contains polynucleotides encoding the receptor, or if the claim encompasses all polynucleotide sequences that encode the receptor. Therefore, the metes and bounds of the claim are unclear. Applicant argues that the term is defined in the specification such that the LBD is derived from the 300 amino acid carboxyl terminal half of an intracellular receptor and is the portion of the receptor protein with which a ligand interacts. However, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It is not clear that the term "derived from" imposes the limitation on this claim that the LBD be derived from the carboxy-terminal half of an intracellular receptor. Furthermore, as the rejection set forth, it is not clear whether the term "derived from" imposes a limitation that the LBD be produced directly from the intracellular receptor, as by enzymatic digestion, or must be expressed from a nucleic acid encoding the intracellular receptor. It is not clear whether an LBD based on the sequence of the intracellular receptor meets the limitation of "derived from".

Claim 13 recites the term "selectivity", which is a conditional term and renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific parameters supported by the specification which Applicant considers to be "selective". Applicant argues that there is basis in the Specification for "selectivity" as meaning an altered binding specificity. However, no parameter is provided in the

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specification for the degree of altered binding specificity which would render the fusion protein as having an LBD which has a different from a native LBD, and thus falling within the limitations of the claim. The metes and bounds of the claim cannot be determined.

Claim 5 recites the term "Substantially", which is a relative term and renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific parameters supported by the specification which Applicant considers to be "Substantially". Applicant argues that the addition of the limitation "relative to exogenous or non-natural ligands" renders the claim definite. However, no specific parameters supported by the specification has been added. The activation of the LBD is to be compared "relative to exogenous or non-natural ligands", however, the relative inactivity is still not defined as to give meaning to when an LBD is not substantially activated, thus the metes and bounds of the claim cannot be determined.

Claims 1, 8, 20, 22, 25, 32, 39, 43, 45, 69, 73 recite the term "specifically", which is a relative term and renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific parameters supported by the specification which Applicant considers to be "specifically". Applicant argues that "specifically" is a term of art and that the specification demonstrates how specificity can be determined. However, it is not clear to what degree the nucleotide binding domain must interact with the target nucleotides in order to meet the limitation of "specifically", thus the metes and bounds of the claims cannot be determined. Claims 2-3, 5-7, 9-19, 21, 23-24, 26-31, 33-38, 40-42, 44, 46, 70-72 are rejected insofar as they depend on claims 1, 8, 20, 22, 25, 32, 39, 43, 45, 69, 73.

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Claim 21 is vague and indefinite in the recitation of the terms "KRAB-ERD", "SID-ERD", "(KRAB)₂", etc. There is no definition within the claim to define the protein to which these acronyms refer. Thus, the metes and bounds of this claim cannot be determined. Applicant argues that the terms are defined in the specification, however, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-38, 43-46, 69-73 are rejected under 35 U.S.C. 102(a) as being anticipated by Beerli et al. (1998).

Beerli et al. teaches a general strategy for the rapid production of gene switches. With a family of defined zinc finger domains recognizing sequences of the 5'-GNN-3' subset of a 64-member zinc finger alphabet, polydactyl proteins specifically recognizing novel 9- or 18-bp sequences were constructed and characterized. Potent transcription factors were generated and shown to control both gene activation and repression. Gene activation was achieved by using the herpes simplex virus VP16 activation domain and a recombinant tetrameric repeat of its minimal

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activation domain. Gene repression or silencing was achieved by using three effector domains of human origin, the Kruppel-associated box (KRAB) (5), the ERF repressor domain (ERD) (12), and the mSIN3 interaction domain (SID) (Beerli at 14628).

Beerli et al. teaches the construction of zinc finger-effector domain fusion proteins, DNAs encoding amino acids 473–530 of the ets2 repressor factor (ERF) repressor domain (ERD), amino acids 1–97 of the KRAB domain of KOX1 (5), or amino acids 1–36 of the Mad mSIN3 interaction domain (SID) were assembled from overlapping oligonucleotides by using Taq DNA polymerase (Beerli at 14629). Beerli et al further teaches polydactyl proteins assembled, from predefined building blocks, to bind a single site in the native erbB-2 promoter. Beerli et al. generated and characterized a family of zinc finger domains that bind each of the 16 5'-GNN-3' DNA triplets, thus claims 1-3, 5-14, 20-27, 32-38, 43-46, 69-73 are anticipated. Beerli et al. further teaches that To examine gene-specific activation, transcriptional activators were generated by fusing the zinc finger protein to amino acids 413–489 of the herpes simplex virus VP16 protein (4), or to an artificial tetrameric repeat of VP16's minimal activation domain, DALDDFDLML (14), termed VP64 (Beerli at 14632), thus claims 15-19 are anticipated. Beerli et al. further teaches that HeLa cells were transfected with effector plasmid (zinc finger constructs in pcDNA3) (Beerli at 14629) thus claims 28-31 are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-35, 37-46, 69-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beerli et al. (1996).

Beerli et al. teaches a general strategy for the rapid production of gene switches. With a family of defined zinc finger domains recognizing sequences of the 5'-GNN-3' subset of a 64-member zinc finger alphabet, polydactyl proteins specifically recognizing novel 9- or 18-bp sequences were constructed and characterized. Potent transcription factors were generated and shown to control both gene activation and repression. Gene activation was achieved by using the herpes simplex virus VP16 activation domain and a recombinant tetrameric repeat of its minimal activation domain. Gene repression or silencing was achieved by using three effector domains of human origin, the Kruppel-associated box (KRAB) (5), the ERF repressor domain (ERD) (12), and the mSIN3 interaction domain (SID) (Beerli at 14628).

Beerli et al. teaches the construction of zinc finger-effector domain fusion proteins, DNAs encoding amino acids 473–530 of the ets2 repressor factor (ERF) repressor domain (ERD), amino acids 1–97 of the KRAB domain of KOX1 (5), or amino acids 1–36 of the Mad mSIN3 interaction domain (SID) were assembled from overlapping oligonucleotides by using

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Taq DNA polymerase (Beerli at 14629). Beerli et al further teaches polydactyl proteins assembled, from predefined building blocks, to bind a single site in the native erbB-2 promoter. Beerli et al. generated and characterized a family of zinc finger domains that bind each of the 16 5'-GNN-3' DNA triplets. Beerli et al. further teaches that to examine gene-specific activation, transcriptional activators were generated by fusing the zinc finger protein to amino acids 413–489 of the herpes simplex virus VP16 protein (4), or to an artificial tetrameric repeat of VP16's minimal activation domain, DALDDFDLDM (14), termed VP64 (Beerli at 14632). Beerli et al. further teaches that HeLa cells were transfected with effector plasmid (zinc finger constructs in pcDNA3) (Beerli at 14629).

Beerli et al. also teaches that novel DNA-binding proteins generated in this manner should have potential utility in DNA-based diagnostic applications. Thus it would have been obvious to one of skill in the art at the time the invention was made to use the nucleic acids encoding the fusion proteins of Beerli et al. in a method of gene therapy. The motivation is provided in Beerli et al. (Beerli at 14633) which states that These proteins might also be used in gene therapy applications to inhibit the production of viral gene products or to activate genes involved in fighting disease. Significantly, the ease with which these proteins can be prepared will facilitate the testing of these ideas by the scientific community.

Conclusion

No claim is allowed.


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Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
October 30, 2002